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Seizure suggestibility may not be an exclusive differential indicator between psychogenic and partial complex seizures: the presence of a third factor

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Differential diagnosis between psychogenic or ('hysterical') pseudoseizures and clinical partial complex seizures has often employed an index or inference of suggestibility. However, recent research indicates a moderate association between complex partial epileptic-like signs and hypnotic capacity in the normal population as well as for complex partial epileptic patients. Consequently, the precipitation of overt, non-stereotyped seizures by instruction may not be a reliable diagnostic method when an insidious process is slowly elevating temporal/limbic lobe lability. Implications for treatment and contra-indication of antipsychotic (D2 antagonist) drugs are discussed.

Key words: pseudoseizures; partial complex seizures; epileptics; hypnosis; differential diagnosis.

Discrimination between complex partial seizures (particularly those with foci within the mesiobasal temporal and limbic lobes) and psychogenic (pseudo or 'hysterical') seizures is frequently based upon the clinical response to suggestion, the absence of extreme stereotypy in the overt motor sequence, no conspicuous neurological indicator and an ambiguous or normal cortical EEG[1–3]. The frequent concurrence of psychogenic seizures and complex partial (with or without secondary tonic–clonic) seizures by the same patients has been attributed to either learning (conditioning) or to secondary gain[4,5]. Recent research[6,7] suggests an alternative interpretation that would significantly influence both the pharmacologocial treatment and diagnosis of patients who exhibit psychogenic seizures.

The relationship between: (1) the shift from experiential and subtle but quantitative electroencephalographic patterns to crudely overt stereotyped and qualitatively conspicuous EEG profiles[8] and (2) the relative numbers of amygdalohippocampal neurons that are recruited into a single paroxysmal discharge[9] has been shown directly. Intracortical monitoring of patients with diagnosed complex partial epilepsy indicated that no obvious experiential change was reported when less than 7% of the sampled neurons exhibited coherent activity while altered consciousness ('subclinical seizures'), that was clearly discriminable to the patient, occurred when approximately 14% of the neurons exhibited simultaneous paroxysmal activity. Commensurate with the 'critical mass' concept of Goldensohn[10], overt stereotyped motor sequences and generalized EEG signatures only became evident when a 'threshold', in this setting an excess of 25% of the neurons were paroxysmal, occurred.

The existence of a continuum of electrical lability within the temporal and limbic lobes has been implied by terms such as Kenneth Livingston's[11] para-epileptic syndrome, epileptic spectrum disorder[12] and complex partial epileptic-like signs (CPELS) continuum[6,13]. Normal volunteers and patients whose subjective experiences and symptoms met the criteria of these labels displayed *quantitative* increases in the signs and symptoms that are

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exhibited by patients with verified, traditional partial (complex) seizures[6,13,14]. The experiences include 'rising sensations' along the alimentary canal, vibrations within the body when falling asleep, transient visual anomalies along the upper lateral peripheral visual field, odd smells, metallic tastes, intermittent depersonalization (or de-realization) and the experience of a presence. Overt displays, as reported by observers, include occasional staring spells or complex mannerisms with substantial individual variability. Both patients who have been just diagnosed (before medication) with partial complex seizures (stereotypic EEG and/or tonic–clonic convulsions) or who ultimately *were* diagnosed after a protracted history of psychiatric referrals, exhibit extremely frequent incidence of these symptoms[6,15].

Patients in whom these symptoms are subjectively or vocationally incapacitating have often sustained mild to moderate closed head injuries[16], experienced periods of hypoxia or hyperthermia or have been exposed to a conspicuous intermittent sequence of stress that would encourage electrical kindling[17,18]. Because these patients rarely exhibit stereotypy with secondary convulsions, incontinence or traditional EEG profiles, they are referred for psychiatric or psychological consideration where neuroleptics are the drugs of choice. However, several studies have shown that subjective phenomenology as well as objective performance deficits (such as disruptions in corpus callosal processing for simultaneously presented auditory input[19]) are remarkably responsive to carbamazepine and remain refractory to D2 blockers. These patients also exhibit theta bursts, which are more quantitatively evident than qualitatively distinct over the temporal regions.

There is now strong evidence that *suggestibility*[20] or 'hypnotizability' is moderately associated with complex partial epileptic-like signs within populations who do not (as yet) exhibit neurological criteria for partial complex epilepsy with foci in the temporal/limbic lobes. Moderate (0.60) strength correlations exist between hypnotic induction profiles (HIP) and the numbers of signs and symptoms of temporal lobe indicators that were collected days to weeks before or after the tests of suggestibility[21,22]. Normal volunteers who exhibit complex partial epileptic-like experiences that are more than two standard deviations above the mean will clearly comply with instructions to perform body movements (e.g. elevation of the arm) as well as pelvic rocking and partial amnesia. Although normal men and women are equally suggestible according to objective criteria, the correlation between suggestibility and complex partial epileptic-like signs (particular for *right* hemispheric indicators) is significantly stronger for women than for men. Not surprisingly, non-pathological but synchronous cortical activity over the temporal (T3/T4) but not the occipital lobes (01/02) is associated with elevated partial complex epileptic-like signs[8,23]. Specific theta bursts over the right but not left temporal lobe are strongly associated with the experience of a presence and the sensation of 'ego-alien' intrusions[24,25].

The documentation of the association between complex partial epileptic-like signs and suggestibility has immediate significance for the validity of the usual strategy for differential diagnosis. 'Induction' of seizures by telephone or by instruction during clinical interview is considered diagnostic of hysterical or 'psychogenic' aetiology[26,27]. However, if some process, particularly an insidious change, has elevated electrical lability within the temporal and limbic lobes, enhanced suggestibility and response to instructions should be an *early symptom* of this change. Whether or not the lability progresses to clinical seizures would depend upon the insidious characteristics of the source (e.g. tumor, focal degeneration).

From this context, the high incidence of concordance between pseudoseizures and classic seizures in epileptic patients would be predictable and would reflect a third factor: numbers of simultaneously discharging neurons within the temporal and limbic (including orbitofrontal/anterior cingulate) lobes. Clinical observation of stereotypy in both EEG and overt displays would occur only when the coherence of paroxysmal activity recruited a critical 'number' of neurons and the enhanced discharge accessed neuropathways that involved cerebral cortical neurons. If this condition did not occur, the paroxysmal activity would remain localized[9] or access more diverse tract systems in less extreme volleys that would encourage greater variability in the external manifestation. That routine access to cortical neurons is not common is indicated by the approximately 50% of patients[28] who have been diagnosed with verifiable partial seizures and who do not exhibit discriminable inter-ictal signatures at the time of measurement and the multiple examples of focal subcortical limbic

seizures during normal cortical EEG activity[29]. It is now clear that subtle biochemical switch (particularly those mediated by situation-specific elevations in CRF and ACTH levels) in the normal matrix of multiple neurotransmitters (during 'stress')[30,31] within the same neuropathways can exert powerful influences upon which discrete routes are accessed by the neuronal volleys.

An underlying continuum of neuronal lability that encourages individualistic (variable) motor sequences with semi-purposeful content within socially specific contexts and non-traditional EEG abnormalities challenges the simple dichotomy of 'true' seizures from 'non-epileptic seizures'. As aptly stated by Doanne[11], it is dangerous to assume that behaviour is purely psychological just because it is strange. Semi-purposeful movements as well as thrashing and pelvic rocking occurs with direct stimulation of the cingulate region and are common correlates of complex partial seizures with frontotemporal foci[32–36]. More than 70% of patients who exhibit psychogenic seizures (without verified seizures) also show either inter-ictal EEG abnormalities, neuropsychological impairment or MRI/CT abnormalities. Commensurate with the concept of an underlying continuum of neuronal lability is the observation that the most predominant prodrome (depression) to psychogenic seizures[37] is also the most common phenomenology of partial complex epilepsy with temporal lobe foci[38].

The second implication involves medication. When pseudoseizures are diagnosed by their verbal induction or by their non-stereotypic pattern, neuropsychiatric referral is common. Because of the schizotypal-like syndromes that are exhibited by many of these patients, neuroleptic drugs such as the phenothiazines and butyrophenones are frequently prescribed. Both animal models of limbic epilepsy and clinical trials indicate that cholinergic rebound during normal serum fluctuations[39] or *intermittent* non-compliance by patients may exacerbate subclinical seizures and reduce seizure thresholds. Limbic cholinergic hypersensitivity has been considered a primary aetiology for subclinical as well as partial complex seizures because of the vulnerability of this system to kindling[40]. Even traditional D2 blockers which often encourage D1 stimulation of the mesolimbic system can initiate kindling[41] which is now seriously considered as one mechanism by which schizophreniform disorders can emerge[42]. Consequently, psychiatric referral and pharmacological intervention may not be necessarily the optimal routine option for these patients.

The fact that most patients who exhibit idiopathic partial or tonic–clonic seizures ultimately show a structural lesion[43] and more than 50% of patients who were diagnosed with 'conversion reactions'[44] also ultimately exhibit neuropathology emphasizes the existence of a continuum of limbic electrical lability. As the source activates more and more of this continuum the presenting symptoms shift from a marked 'conscious' and variable neurological profile to an unambiguous stereotypy of both EEG and clinical indicators. The existence of this continuum and its relationship with suggestibility indicates that patients who: (1) exhibit pseudoseizures in response to suggestion *and* (2) exhibit marked elevation in the quantitative incidence of signs and symptoms that are associated with partial complex epileptic foci, should be evaluated periodically.

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